

Nutritional Analysis of Extremely Preterm Infants with Bronchopulmonary Dysplasia

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Chapter 1

Introduction

Bronchopulmonary Dysplasia (BPD), a chronic lung disease, is a significant problem in preterm infants, especially the extremely preterm. BPD is defined as the need for oxygen at 28 days of life to maintain adequate oxygenation (Jobe & Bancalari, 2001). It is estimated that 10,000-15,000 preterm infants develop BPD each year with $\frac{2}{3}$ of these infants born at less than 28 weeks gestation (Bland, 2004; Lemons et al., 2001; National Vital Statistics Reports, 2002). BPD results from the interaction of developmentally immature lungs and the use of ventilatory and oxygen strategies to manage acute respiratory distress. These strategies have been successful in improving the survival rates of extremely preterm infants. Unfortunately, the increased survival of extremely preterm infants has resulted in a parallel increase in the incidence of BPD. The numbers of preterm infants who develop BPD will continue to increase as greater numbers of extremely immature infants survive acute respiratory disease (Berger, Bachman, Adams, & Schubiger, 2004; Bancalari et al., 2003).

Growth is considered one of the most important therapies for preterm infants with BPD since lung growth and development occurs as physical growth occurs. Experts believe that improvement in growth will improve lung growth and decrease the severity of the BPD (Biniwale & Ehrenkranz, 2006). Unfortunately, inadequate growth is one of the most common morbidities affecting preterm infants with BPD (Lemons et al., 2001).

One of the most important strategies to improve growth is to provide adequate nutrition to these infants. All extremely preterm infants are difficult to nourish during the early weeks of life and thus develop a growth deficit during this time that persists until discharge from the neonatal intensive care unit (Bloom et al., 2003; Clark et al., 2003). This significant clinical problem is even more pronounced in preterm infants who ultimately develop BPD (Ehrenkranz et al., 1999; Radmacher, Looney, Rafail, & Adamkin, 2003; Steward, Armbruster, & Lennie, in press). Preterm infants with BPD are difficult to nourish throughout hospitalization. The purpose of this study was to describe the nutrition deficits that preterm infants with BPD cumulate across hospitalization.

Chapter 2

Review of Literature

Because more preterm infants are surviving, growth has become an important issue not only in terms of physical growth, but adequate growth is important for the continued development of extremely immature lungs. As a result of preterm birth, lung development must occur in the extrauterine environment while also participating in gas exchange (Jobe, 2002). The inadequate growth that is associated with BPD can have important consequences for pulmonary outcomes. An important factor limiting the growth potential of the immature lungs is poor physical growth (Massaro & Massaro, 1996). McEvoy and colleagues (2003) demonstrated that preterm infants with BPD had significantly reduced lung volumes when compared to stable preterm infants. Clearly, underlying growth outcomes is adequacy of nutritional intake. Researchers have demonstrated that undernutrition in a preterm rabbit model resulted in interference with lung development and slow growth velocity when compared to nourished preterm rabbits (Mataloun, Rebello, Mascaretti, Dohnnikoff, & Leone, 2006). Further, in a sub-group of preterm rabbits, the interaction of undernutrition and use of oxygen exacerbated the alterations in lung development.

Growth. Inadequate growth in preterm infants with BPD is well established during the early weeks of life, prior to the diagnosis of BPD (Bloom et al., 2003; Steward

et al., in press). Researchers have demonstrated that, by 14 days of life, the growth of preterm infants who developed BPD differed significantly from the growth of stable preterm infants (deRegnier et al., 1996; Ehrenkranz et al., 1999; Khan, Kuzma-O'Reilly, Brodsky, & Bhandari, 2006). When compared to ideal or expected weight gain, the actual weight gain of preterm infants with BPD during the first 28 days of life differed significantly from ideal weight gain (Karn & Steward, 2005). These differences in growth persist throughout hospitalization. The continued weight gain of preterm infants with BPD lags several weeks behind that of a relatively stable preterm infant with the same birthweight (Ehrenkranz et al., 1999). In a large study of growth in extremely preterm infants, the highest percentage of preterm infants developing BPD was found in the two lowest quartiles (Ehrenkranz et al., 2006). By discharge, preterm infants with BPD have developed a significant growth deficit with attained weights well below the 10th percentile (Ehrenkranz et al., 1999; Radmacher, Looney, Rafail, & Adamkin, 2003).

The current goal for minimum growth for all preterm infants is to gain weight at a rate that mimics the intrauterine rate of growth for a fetus, 15 gms/kg/day (Ziegler, Thureen, & Carlson, 2002). Because preterm infants with BPD begin life acutely ill and progress to chronic lung disease, achieving the desired rate of weight gain does not occur until the infant is several weeks old. Even then, the rate of weight gain has been found to be less than 15 gms/kg/day (Ehrenkranz et al., 1999; Guzmán et al., 2001; Karn & Steward, 2005; Kulkarni, Ehrenkranz, & Bhandari, 2006).

Nutritional Intake. Preterm infants with BPD are at risk for undernutrition due to difficulties maintaining appropriate nutritional intake as a result of co-morbidities (Carlson, 2004), medically indicated fluid restriction (Carlson, 2004; Oh et al., 2005), and

elevated energy expenditure (Bauer et al., 2003; Leitch & Denne, 2000). Most importantly, there is a lack of empirical evidence to support suggested recommendations for nutritional intake (Lai, Rajadurai, & Tan, 2006; Reynolds & Thureen, 2007). These infants present a major challenge in achieving optimal nutritional intake at two time points, early in life during acute illness and after achieving stabilization of respiratory function. Researchers have demonstrated that preterm infants with BPD receive significantly fewer calories than stable preterm infants during the first weeks of life (deRegnier et al., 1996; Guzmán et al., 2001; Lee & Yu, 1996; Steward et al., in press). Khan et al. (2006) demonstrated that preterm infants with BPD received 16% less calories during the first month of life when compared to stable preterm infants.

Following respiratory stabilization, the goal of nutritional intake is to promote growth. The usual standard of care is to add modular components to preterm formula or breast milk to increase the nutrient value in order to overcome nutritional obstacles and stimulate growth (Carlson, 2004; Puangco & Schanler, 2000). The goal is to achieve at least 120 kcal/kg/day, with recommendations for even higher intake (REF). Researchers demonstrated that preterm infants with BPD rarely achieved 120 kcal/kg/day and when this goal was achieved it was not maintained (Kulkarni et al., 2006; Radmacher et al., 2003).

In comparing actual nutritional intake during the first 28 days of life to recommended caloric and protein intake, researchers demonstrated that preterm infants with BPD received significantly fewer calories and grams of protein and developed significant energy and protein deficits by 28 days of life. The mean caloric intake was 98.6 kcal/kg/day by day of life 28. The preterm infants had a cumulative energy deficit

of 598 kcal/kg by the end of 28 days (Karn & Steward, 2005). From the above findings, preterm infants with BPD are undernourished early in life.

Chapter 3

Research Methods

This study is a part of a larger study focused on the systemic effects of inflammation on the growth of preterm infants with BPD. The purpose of the current study was two-fold: 1) to analyze the caloric and protein composition of nutrition provided to preterm infants with BPD and compare the nutrition composition to the standard recommended intake of these nutrients for preterm infants as well as the recommendation for those with BPD and 2) to describe the cumulative nutrient deficits in these infants across hospitalization. It was hypothesized that these extremely preterm infants with BPD will receive less than the usual recommended requirements of caloric and protein intake as well as the recommended intake for BPD infants. Several research questions were also addressed:

- 1) What is the caloric and protein intake per kilogram for day 28 of life through 36 weeks post-conceptual age and how does it compare to the recommended requirements?
- 2) What type of cumulative nutrient deficit is developed by these infants?
- 3) How is the rate of growth for these infants affected by these nutrient deficits in comparison to ideal growth rates?

The target population for this study is extremely preterm infants (those born before 29 weeks gestational age). A convenience sample of 28 infants was obtained from The Ohio State University Medical Center Neonatal Intensive Care Unit (NICU).

Inclusion criteria included:

1. Less than 29 weeks gestational age
2. Males and females
3. Birthweight appropriate for gestational age (between 11th and 89th percentiles) using the fetal growth parameters developed by Alexander et al. (1996).
4. Continued need/requirement for ventilatory support and/or oxygen supplement at 28 days of life.
5. 75% of nutritional intake obtained through enteral nutrition
6. No signs of infection

Exclusion criteria included:

1. Major congenital anomalies or malformations, especially respiratory, cardiac, gastrointestinal, or oral structures
2. Pulmonary hemorrhage
3. Anoxic brain injury at birth
4. Small for gestational age (birthweight <10th percentile)
5. Large for gestational age (birthweight >90th percentile)
6. Hemodynamically significant patent ductus arteriosus Clinical and laboratory evidence of sepsis
7. Death
8. Major surgery

9. Majority of nutrition received parenterally

10. Clinical signs of NEC

Because this study is looking at extremely preterm infants as its research subjects, the Ohio State University Institutional Review Board (IRB) needed to review the research proposal regarding human subjects concerns. After review, the study was approved for implementation. Measures were taken to ensure the participants and their parents have the right not to be harmed, the right of self-determination, the right to full disclosure, and the right of privacy, confidentiality, or anonymity.

Infants were recruited from the Ohio State University Medical Center NICU. The eligibility of potential study infants was determined by the nursing staff or Attending Neonatologist in the NICU. Parents of eligible infants initially were approached by these nurses to determine if they would be interested in learning more about the study. Names of interested parents were provided to a member of the research team who explained the study, answered all questions, and obtained informed written consent. Parents were assured that they may withdraw their infant from the study at any time and that in doing so would in no way affect the medical and nursing care of their infant. Data gathered in this study were used for research purposes only. All research materials were identified by a code number and were kept locked in a research office in a locked file cabinet. No one other than the investigators and study personnel had access to the data.

Growth Analysis. Growth data for this study were abstracted from the infant's medical records. Daily weight was the growth parameter used for this study because all clinical decision-making is based on daily weights. Daily weights were recorded from day 28 of life through 36 weeks post-conceptual age (PCA). Daily weights were used

to calculate growth velocity, defined as grams of weight gain per kilogram per day (gms/kg/day). This will be determined by dividing the total weight gain in grams for the study period by the number of days in the study period and then dividing by average body weight in kilograms for the study period.

Nutritional Analysis Nutritional data for this study were abstracted from the infants' charts. Daily records of type and amount of enteral nutrition were obtained from 28 days of life until each infant reached 36 weeks PCA. Using NEONOVA®, nutritional software specifically designed to analyze nutritional intake of infants in the NICU, the obtained nutritional intake was analyzed for caloric and protein composition. Daily and cumulative caloric and protein deficits were calculated based on the standard recommendation of 120 kcal/kg/day and 3 gms protein/kg/day and the recommended intake for BPD at 135 kcal/kg/day and 4 gms/protein/kg/day (Biniwale & Ehrenkranz, 2006).

Chapter 4

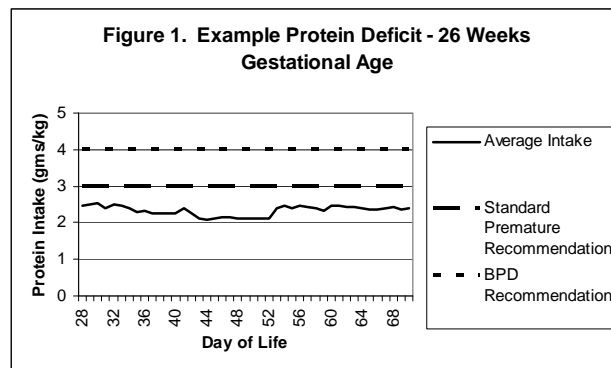
Results

The sample was comprised of 28 preterm infants from the NICU. The mean gestational age at birth for these infants was 25.76 weeks. The mean birthweight for the 28 infants was 913.21 grams and the mean weight at 36 weeks PCA was 2031.41 grams. The most common type of enteral nutrition received by these infants was fortified human breast milk, with 74% of the infants receiving this at 28 days of life and 57% receiving it at 36 weeks PCA. The next most common type of enteral nutrition was Similac Special Care formula with 22% receiving this at 28 days of life and at 36 weeks PCA.

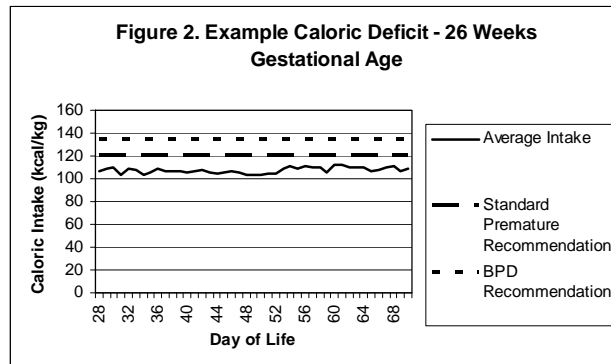
In Table 1 the average caloric and protein intake and average growth velocity are presented for each gestational age and for all of the infants as a group. The cumulative deficits are also presented for calories and protein in comparison to the standard recommendations for preterm infants and those preterm infants with BPD.

As a group the infants had an impressive cumulative caloric deficit of 904.07 kcal/kg and 54.33 gms of protein/kg in relation to the

recommendations for those preterm infants with BPD. Figures 1 and 2, using the infants born at 26 weeks gestational age as an example, provide a comparison of actual average



daily intake to the standard recommendations for preterm infants and those recommendations for those infants with BPD. In addition, the weekly weight gain was plotted on the fetal infant growth chart along with the ideal growth rate for the infants born at 26 weeks gestational age (See Appendix A).



Comparison of All Infants							
Gestational Age	29 Weeks	28 Weeks	27 Weeks	26 Weeks	25 Weeks	24 Weeks	All Infants
Average Caloric Intake (cal/kg/day)	115.53	108.67	107.88	106.92	89.68	102.26	105.16
Average Protein Intake (gm protein/kg/day)	3.1	2.57	2.41	2.35	1.44	2.36	2.37
Cumulative Caloric Deficit - Standard Recommendations	65.67 (±60.71) range 11-131	328.6 (±340.37) 77-918	441.83 (±275.82) -11-789	430.13 (±325.93) 79-912	1152 (±0) 1152	1002 (±56.57) 962-1042	570.04 (±418.08)
Cumulative Caloric Deficit - BPD Recommendation	371.33 (±26.31) 341-388	763.6 (±340.37) 512-1353	921.83 (±271.78) 529-1299	927 (±431.44) 289-1557	1722 (±0) 1722	1702 (±98.99) 1632-1772	1067.96 (±538.32)
Cumulative Protein Deficit - Standard Recommendations	3.33 (±13.82) -4.06-19.27	12.61 (±9.37) 2.14-21.28	23.81 (±26.77) -12.46-51.31	27.73 (±26.99) -4.96-63.57	59.42 (±0) 59.42	34.8 (±34.32) 10.53-59.07	26.95 (±19.44)
Cumulative Protein Deficit - BPD Recommendations	12.33 (±8.73) 2.27-17.94	41.61 (±9.37) 31.14-50.28	54.47 (±25.78) 23.42-85.31	55.85 (±32.14) 13.83-106.57	97.42 (±0) 97.42	120.8 (±10.93) 113.07-128.53	63.75 (±39.17)
Average Growth Velocity (gm/kg/day)	16.56	10.37	13.76	13.95	10.63	17.88	13.86

Table 1. Growth and Nutritional Analyses.

Chapter 5

Discussion

The purpose of this study was to examine the nutritional content of enteral nutrition in these preterm infants with BPD and compare it to the standard recommended values for preterm infants and those recommendations for infants with BPD, as well as look at how growth patterns of these infants. Daily weights as well as daily accounts of type and amount of enteral nutrition were obtained from the 28 infants' charts. Using NEONOVA® software, nutritional content of the enteral nutrition was computed in kcal/kg and grams of protein/kg. These values were compared to the recommended values to look at daily and cumulative deficits. Growth velocities were also calculated.

As can be seen in Table 1 and in Figures 1 and 2, the graphs of the caloric and protein deficits in the example 26 week gestational age group, the average daily intake of both calories and protein across all of the gestational ages was well below the recommended values. This resulted in substantial cumulative deficits throughout their hospitalization. These huge cumulative deficits affect these infants growth throughout their hospitalization (see Appendix A), and also affect their growth after discharge (Binwale & Ehrenkranz, 2006, Ernst, et al., 2003). This malnutrition also has a significant affect on the pulmonary development of these infants, and contributes to the development and progression of BPD. An important question worth asking is whether these nutrient deficits contributed to the prolonged need for oxygen. Studies have shown

that the combination of prolonged oxygenation and under nutrition has detrimental effects on these already underdeveloped lungs, but whether the under nutrition causes the need for the oxygenation is not known (Mataloun et al., 2005).

Many studies have been done regarding this problem of under nutrition in these extremely preterm infants. Maintaining adequate nutritional intake in these infants is difficult when the many other complications and morbidities unique to these extremely preterm infants are factored in. Adequate nutrition is known to result in better growth outcomes and to be very beneficial in the development of the preterm lung (Dinerstein et al., 2005; Jobe, 2006). However, while we know these infants have deficits at discharge, the full extent of their cumulative deficit acquired throughout their hospitalization has not been examined. This study began to look at that cumulative deficit, and it is evident that it is a remarkable issue. A limitation of the study included the fact that obtaining a full nutritional collection from day of birth would help fully grasp the deficit these infants are experiencing. Gathering information regarding the decision making when calories are increased or formula is changed is also very important to understand the reasoning behind this under nutrition.

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Appendix A

FETAL-INFANT GROWTH CHART FOR PRETERM INFANTS

